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Differences in function and recovery profiles between patterns of multimorbidity among older medical patients the first year after an acute admission—An exploratory latent class analysis

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ABSTRACT

Introduction: Multimorbidity is common among older people and may contribute to adverse health effects, such as functional limitations. It may help stratify rehabilitation of older medical patients, if we can identify differences in function under and after an acute medical admission, among patient with different patterns of multimorbidity.

Aim: To investigate differences in function and recovery profiles among older medical patients with different patterns of multimorbidity the first year after an acute admission.

Methods: Longitudinal prospective cohort study of 369 medical patients (77.9 years, 62% women) acutely admitted to the Emergency Department. During the first 24 h after admission, one month and one year after discharge we assessed mobility level using the de Morton Mobility Index. At baseline and one-year we assessed handgrip strength, gait speed, Barthel20, and the New Mobility Score. Information about chronic conditions was collected by national registers. We used Latent Class Analysis to determine differences among patterns of multimorbidity based on 22 chronic conditions.

Results: Four distinct patterns of multimorbidity were identified (Minimal chronic disease; Degenerative, lifestyle, and mental disorders; Neurological, functional and sensory disorders; and Metabolic, pulmonary and cardiovascular disorders). The “Neurological, functional and sensory disorders”-pattern showed significant lower function than the “Minimal chronic disease”-pattern in all outcome measures. There were no differences in recovery profile between patients in the four patterns.

Conclusion: The results support that patients with different patterns of multimorbidity among acutely hospitalized older medical patients differ in function, which suggests a differentiated approach towards treatment and rehabilitation warrants further studies.

1. Introduction

Functional decline relating to acute illness and hospitalization is a common phenomenon in older adults (Boyd et al., 2008; Brown, Friedkin, & Inouye, 2004; Covinsky et al., 2003; Mudge, O'Rourke, & Denaro, 2010; Oakland & Farber, 2014; Zaslavsky, Zisberg, & Shadmi, 2015; Zisberg, Shadmi, Gur-Yaish, Tonkikh, & Sinoff, 2015). Functional decline refers to a declining ability to perform activities that ensure one's independence, such as rising unaided from a chair (Inouye et al., 1993). Several studies find that acute medical hospitalization of older

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patients is associated with functional decline and loss of independence (Kortebein, 2009; Krumholz, 2013) and that low mobility during hospitalization is a contributing factor (Brown et al., 2004; Zisberg, Shadmi, Sinoff, Gur-Yaish, & Srulovici, 2011, 2015). Additionally, studies have found that this decline may persist up to one year after discharge (Boyd, Xue, Guralnik, & Fried, 2005, 2008; Brown et al., 2009; Gill, Allore, Gahbauer, & Murphy, 2010; Gill, Gahbauer, Murphy, Han, & Allore, 2012; Zisberg et al., 2015). In contrast, some studies have found an improvement in function during and after an acute hospitalization (Bodilsen et al., 2013; Moen, Ormstad, Wang-Hansen, & Brovold, 2018; Muller et al., 2007). The effect of hospitalization on function among older acutely admitted patients is therefore unclear. Maintaining independent function is essential for performing activities of daily living (ADL) in older adults and hence, independent living, which for many older adults is considered the most important health outcome (Fried et al., 2011; Groessl et al., 2007). Identifying which patients experience functional decline after an acute hospitalization is therefore of importance.

Multimorbidity, the co-occurrence of two or more chronic conditions within an individual (Akker, van den Buntinx, & Knottnerus, 1996; Nicholson et al., 2018), is now the norm in the aging population, due to medical advances and the increasing mean life expectancy (Barnett et al., 2012). Multimorbidity is associated with polypharmacy (Aoki, Yamamoto, Ikenoue, Onishi, & Fukuhara, 2018; Mannucci, Nobili, & REPOSI Investigators, 2014), poor health-related quality of life (Fortin et al., 2006; Tyack et al., 2016), mortality (Gijsen et al., 2001; Nunes, Flores, Mielke, Thumé, & Facchini, 2016), increased consumption of health resources (Cassell et al., 2018; Salisbury, Johnson, Purdy, Valderas, & Montgomery, 2011; Wolff, Starfield, & Anderson, 2002), frailty (Vetrano, Palmer et al., 2018) as well as low physical functioning (Garin et al., 2014; Marengoni, Angleman, Melis et al., 2011; Marengoni, von Strauss, Rizzuto, Winblad, & Fratiglioni, 2009).

Patients with multimorbidity do not constitute a homogeneous group (Guiding Principles for the Care of Older Adults with Multimorbidity: An Approach for Clinicians, 2012), which is why subgrouping of patients with multimorbidity may be useful when assessing the influence of acute hospitalization on function. Patterns of multimorbidity refer to the classification of chronic diseases into different disease combinations or patterns based on associations between the chronic conditions. Recently, research has been focused on the development of multimorbidity patterns as a way of understanding the complexity that characterizes older medical patients (Guisado-Clavero et al., 2018a; Nguyen, Wu, Odden, & Kim, 2018; Prados-Torres, Calderón-Larrañaga, Hancco-Saavedra, Poblador-Plou, & van den Akker, 2014). Specific combinations of chronic conditions could have an effect on physical function that goes beyond the sum of the effect of the individual chronic conditions (Fried, Bandeen-Roche, Kasper, & Guralnik, 1999). Several studies have examined the associations between different patterns of chronic diseases and function (Garin et al., 2014; Jackson et al., 2015; John, Kerby, & Hagan Hennessy, 2003; Marventano et al., 2014a; Olaya et al., 2017; Quiñones, Markwardt, & Botoseneanu, 2016, 2018; Vetrano, Rizzuto et al., 2018) and found that patterns including a psychiatric disorder such as depression are associated with lower function. However, studies that investigate the associations between multimorbidity and objective measures of function are sparse and only included a few chronic conditions (Vetrano, Rizzuto et al., 2018). As patients admitted in the Emergency Department have many different chronic conditions, and these often are correlated, we chose to model the association between chronical conditions and function by latent class models. Being able to generate new hypotheses by modelling how different patterns of multimorbidity relate to function among acutely hospitalized older medical patients using objective measures of functional performance, may potentially help stratify patients for rehabilitation and research and improve the outcome after an acute admission. Therefore, this study aimed to investigate differences in function and recovery profiles among older medical patients with different patterns of multimorbidity the first year after an acute admission.

2. Methods

2.1. Setting and design

In Denmark, a public healthcare system provides feeless, tax-paid treatment for primary medical care, hospitals, and home care services uniformly for all citizens. This exploratory study was performed as a part of the Disability in older medical patients (DISABLMENT) Cohort. This cohort aimed to study the ability of physical performance measures and biomarkers to predict adverse health events following an acute medical hospitalization (Bodilsen et al., 2016; Klausen et al., 2017). Outcome assessments for the DISABLEMENT cohort were conducted both in the medical section of the 30-bed Emergency Department at Copenhagen University Hospital, Hvidovre, Denmark within 24 h of an acute medical admission and at two follow-up visits in the patients' home one month and one year after discharge. Data on function from the acute admission and the one-month follow-up visit have been reported previously (Bodilsen et al., 2016).

2.2. Population

The inclusion of patients has been described in detail elsewhere (Bodilsen et al., 2016; Klausen et al., 2017). In short, patients were randomly included between July 2012 and September 2013 with follow-up visits in the patients' home one month and one year after discharge. Patients were included if they were acutely admitted to the medical section of the Emergency Department, and 65 years old or older. Patients were excluded if they: were unable to cooperate; had a short length of stay which excluded assessment before discharge; were unable to understand Danish; were transfered to an intensive care unit; were diagnosed with cancer; had a terminal illness; and were in isolation. Patients were randomly selected based on their unique civil registry number using a computer-generated list. A sample of 369 older medical patients were included in the study of which 323 patients participated in the one-month assessment and 250 patients participated in the one-year assessment. Fig. 1 summarizes the inclusion process of the study.

2.3. Outcomes

2.3.1. Chronic conditions

We included 35 chronic conditions for this study based on the open-source Chronic Condition Measurement Guide (Juul-Larsen et al., 2019) (Supplementary S1). The Chronic Condition Measurement Guide is an guide of 83 chronic conditions based on registry data from The Danish National Patient Register (Lynge, Sandegaard, & Rebolj, 2011) derived from persons aged 65 years and older using ten years of history. The 83 chronic conditions were grouped according to their pathophysiology which constituted 35 chronic conditions in the list by a medical specialist in internal medicine. Cancer was excluded from the list as it was one of the exclusion criteria in the DISABLMENT cohort restricting the number of chronic conditions from 35 to 34. To avoid too few observations, the chronic conditions were identified as the 95% most prevalent chronic conditions in the DISABLMENT cohort constituting 22 chronic conditions (Supplementary S2).

2.3.2. Measures of function

Measures of function in the cohort have been described in detail elsewhere (Bodilsen et al., 2016; Klausen et al., 2017). In short, we used several objective and subjective measures of functional capability. The measures were chosen based on their ability to evaluate dependency in function, in both hospitalized older patients and in community-

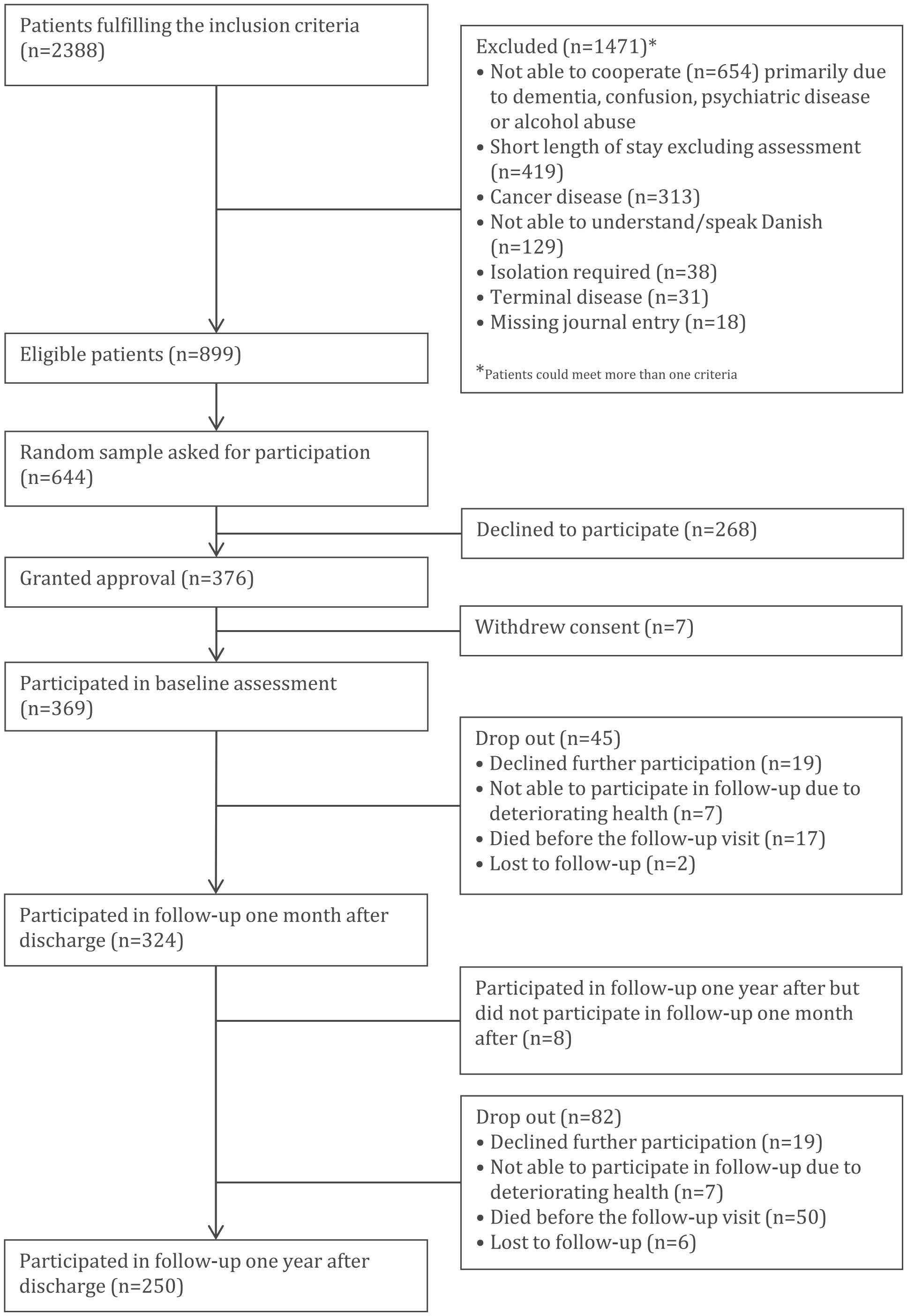

Fig. 1. Flowchart of the inclusion process.

dwelling older patients (Bodilsen et al., 2015, 2016; Cesari et al., 2009; Cooper et al., 2011; den Ouden, Schuurmans, Arts, & van der Schouw, 2011; Gill et al., 2010; Guralnik et al., 1994; Humphreys et al., 2002; Studenski et al., 2003). The primary outcome was the de Morton Mobility Index (DEMMI) (de Morton, Brusco, Wood, Lawler, & Taylor, 2011): The DEMMI is a reliable and valid test to be used in older persons across different health-care settings, i.e., in the community, and during sub-acute and acute hospitalization. Also, the DEMMI score has been developed for objective assessment of mobility in older medical patients. The DEMMI score range from 0 to 100, zero indicate patients being bed bound. The threshold value for independent mobility is 62 (Macri, Lewis, Khan, Ashe, & de Morton, 2012). The minimal clinically important difference on the DEMMI score is 10 points in an older acute medical population (de Morton, Davidson, & Keating, 2008; de Morton, Davidson, & Keating, 2010; Trøstrup, Andersen, Kam, Magnusson, & Beyer, 2001). DEMMI was assessed at all three time points. The secondary outcomes of function were: gait speed; handgrip strength; Barthel20; and the New Mobility Score. The secondary outcomes were assessed at baseline and one year. Gait speed (GS) was assessed over a 4-m. course. GS is a reliable test in older medical patients (Bodilsen et al., 2015). Patients were allowed to use their normal walking aid if one was needed. The faster of two test trials in seconds was used in the analyses. Handgrip strength (HGS) was assessed in the dominant hand using a handheld dynamometer (Saehan, Digi-II). HGS is a reliable test in older medical patients (Bodilsen et al., 2015). Patients were tested with their elbow flexed in a 90 degree angle and the lower arm resting on an armrest. The highest value of minimum three trials were used in the analyses. Barthel20 was used to determine dependency in activities of daily living (Wade & Collin, 1988). The score ranges from 0 to 20 points. Lower scores reflect dependency. New Mobility Score (NMS) was used to determine the patients´ functional independence (Kristensen, Foss, & Kehlet, 2005; Kristensen, Foss, Ekdahl, & Kehlet, 2010). The score ranges from 0 to 9 points. Lower scores reflect functional dependency. Recovery profiles was defined as the change in function from baseline to follow up.

2.4. Descriptive data

Age and sex were based on data from The Danish Civil Registration System (Pedersen, 2011). Drug use was assessed by data from the Shared Medication Card Online, which records all prescribed medication in Denmark (Iversen et al., 2018). Medication was included if it was for systemic use and the given prescription had been redeemed within 120 days of the index admission. The list was condensed to the most recent purchase for each unique ATC code. Prescriptions with end dates before admission or start dates after admission were excluded. Polypharmacy was present if the patient redeemed five or more prescriptions at a pharmacy. Hyperpolypharmacy was present if the patient redeemed ten or more prescriptions at a pharmacy. Reason for admission was reported according to the chapters of the International Classification of Diseases, 10^{th} edition.

2.5. Ethical considerations

All patients received written information about the procedures of the study, and informed consent was obtained in strict accordance with the Declaration of Helsinki. Study approval was granted by The Ethics Committee in Copenhagen (H-1-2011-124 167) and The Data Protection Agency (01596 HVH-2012-005).

2.6. Statistical analyses

The study sample and the patients who dropped out were compared with regards to age, sex and DEMMI using the Chi-squared test and the Kruskal-Wallis test for ordinal and continuous variables, respectively. Data from admission are presented as numbers and percentages or as medians with a corresponding interquartile range (IQR). No sample size estimation was made for the present study while it is an exploratory study in a previously defined cohort. The sample size the DISABLEMENT cohort has previously been reported (Bodilsen et al., 2016).

Patterns of multimorbidity were identified using latent class analysis (LCA). LCA is a method used for data reduction when analyzing multivariate categorical data (Hagenaars, 2009). LCA is based on correlations between the chronic conditions, meaning that chronic conditions can be included in several patterns. We used the two-step estimation of models and external variables as suggested by Bakk et al. (Bakk & Kuha, 2018). Firstly, to determine the best-fitted model a sequence of models was fitted without any explanatory variables (Nylund-Gibson & Masyn, 2016) by increasing the number of classes starting with a two-class model continuing until the sample-size adjusted Bayesian information criterion (BIC) stopped decreasing. We used BIC together with qualitative evaluations of the usefulness and clinical judgment to determine the optimal number of classes (Nylund, Asparouhov, & Muthén, 2007). Entropy was used as a tool to measure the degree of classification uncertainty, i.e., the extent to which the groups were different from one another when assigning individuals into latent classes. An entropy of 0.36, 0.65 and 0.90 represent low-, medium-, and high classification certainty, respectively (Bakk & Kuha, 2018). Due to the large number of parameters we used 15,000 random sets of starting values with 100 iterations per set to ensure that global rather than local maxima of the likelihood function were reached. If the likelihood function was not replicated, we increased the starting values until this criterion was met. After determining the number of classes, we tested for differential item functioning (DIF) concerning sex and age for all 22 items. DIF of an outcome is present when the outcome still depends on an explanatory variable after adjusting for the latent variable (Teresi & Fleishman, 2007). The model should therefore adjust for the DIF and thereby assign different probabilities for a chronic condition in a class depending on whether the explanatory variable is present or not. If DIF was present, it was included in the model. Each latent class corresponds to an underlying subgroup of patients characterized by a pattern of chronic conditions; we will refer to these latent classes as patterns of multimorbidity. The patterns were labeled based on which conditions exhibited excess prevalence (i.e., the prevalence in a class exceeds the prevalence in full cohort with more than ten percentpoints). After fixing the parameter estimates from the measurement part of the latent class model, we fitted a linear regression model (within the latent class model) with the outcomes and tested differences for the outcomes using the Wald test. SAS enterprise guide 7.1 packages (SAS Institute, Cary, NC, USA) were used for data management and analysis of descriptive data and prevalence. Mplus Version 7.1 (Muthén & Muthén, Los Angeles, CA) was used for latent class analysis. Level of significance was set at 0.05.

3. Results

3.1. Attendance and dropout

Attendance and dropouts up until the one-month follow-up visit have been described in detail elsewhere (Bodilsen et al., 2016). In total, 369 patients were included in the cohort of which 324 patients completed the one-month follow-up visit. Eight patients participated in the one-year follow-up but did not participate in the one-month follow-up visit; five patients had declined; two patients could not participate due to deterioration in their health, and one patient was lost to follow-up. Of the 324 patients who participated in the one-month follow-up visit, 82 patients did not participate in the one-year follow-up visit. A flowchart including reasons for dropouts is shown in Fig. 1. In total, 250 patients participated in the one-year follow-up visit.

There were no differences regarding sex and age for patients who dropped out from; baseline to the one-month follow-up or from one-month follow-up to the one-year follow-up compared to the study sample at baseline. There was a significant difference in DEMMI at baseline for patients who dropped out from baseline to the one-month follow-up visit (median: 53 vs. 62, $p = 0.02$) and a non-significant difference for patients who dropped out from the one-month follow-up visit to the one-year follow-up visit (median: 65 vs. 67, $p = 0.06$). There were no differences regarding sex for patients who died from baseline to the one-month follow-up visit nor for patients who died from the one-month follow-up visit to the one-year follow-up visit compared to patients included in the analyses. Patients who died between baseline and one-month were older (median: 86 vs. 78, $p = 0.001$) and had a lower DEMMI-score at baseline (median: 36 vs. 62, $p < 0.001$) than the 324 patients included in the analysis from the one-month follow-up. Patients who died between the one-month follow-up and the one-year follow-up were older (median: 82 vs. 77, $p = 0.03$) and had a lower DEMMI-score at baseline (median: 48 vs. 67, $p < 0.001$) than the 250 patients included in the analysis from the one-year follow-up. A description of the study population is shown in Table 1.

3.2. Determining the optimal number of latent classes

The analysis of patterns of multimorbidity was done on the 369 patients who participated in the baseline outcome assessment. When looking at the relative goodness-of-fit indices, the adjusted BIC-values continued to decrease from two-class to the four-class model but increased the five-class model (the Three-class-model aBIC = 6190, the Four-class-model aBIC = 6189, the Five-class-model aBIC = 6198)

Table 1
Characteristics of the population (n = 369).

Age, years; median (IQR)	78	(71;85)
Female; number (%)	230	(62)
No. of chronic conditions[1]; median (IQR)	4	(2;6)
Multimorbidity[1]; number (%):	311	(84)
Polypharmacy; number (%):	325	(88)
Hyper polypharmacy; number (%):	204	(55)
Length of stay(days); median (IQR)	2	(1;6)
Reason for admission; number (%)		
Respiratory diseases	105	(28)
Symptoms, signs or for observation	66	(18)
Cardiovascular diseases	57	(15)
Endocrine diseases	34	(9)
Genitourinary diseases	30	(8)
Infectious diseases	20	(5)
Musculoskeletal diseases	16	(4)
Other	41	(11)

Note: [1]Based on the full Chronic Condition Measurement Guide containing 83 chronic conditions (Juul-Larsen et al., 2019). Length of stay and Reason for admission are also displayed in Bodilsen et al. (2016).
Abbreviations: IQR = Inter quartile range.

(Supplementary file S3). Parametric bootstrapped likelihood ratio test for two vs. three, three vs. four, and four vs. five classes yielded a p-value of 0.01, 0.02, and 0.05, respectively (Supplementary file S3). By looking at the BIC-values, the bootstrapped test, and clinical judgment, the four-class model was found to have a meaningful clinical interpretation and was chosen as the final model. DIF was investigated for the explanatory variables; age and sex. We found DIF between sex and disorders of the lipoprotein metabolism; mental disorders due to alcohol; osteoporosis/osteoarthritis; and genitourinary diseases, respectively. Additionally, we found DIF between age and diabetes; and obesity, respectively. Entropy was 0.76. The final model included direct effects between the explanatory variable and the items where we found significant DIF.

The estimated probability of having a chronic condition and pattern prevalence based on the latent class analysis are shown in Table 2. The largest pattern was characterized by patients with the low-estconditional probabilities of the 22 chronic conditions when compared with the marginal probabilities in the full cohort. This pattern was labeled *"Minimal chronic conditions"*. The second pattern was characterized by patients with high conditional probabilities of having depression, COPD/asthma, neuropathy, osteoporosis, arthritis, mental disorders due to tobacco and alcohol use, and obesity when compared with the marginal probabilities in the full cohort. This pattern was labeled *"Degenerative, lifestyle and mental disorders"*. The remaining two patterns had the highest expected number of chronic conditions and therefore had the highest burden of multimorbidity; the third pattern was characterized by patients with high conditional probabilities of having dementia, disability, brain infarction, hypertension, osteoporosis, sensory disorder, cardiovascular disease, and non-inflammatory gynecological problems, when compared with the marginal probabilities in the full cohort. This pattern was labeled *"Neurological, functional and sensory disorders"*; the fourth pattern was characterized by patients with high conditional probabilities of having diabetes, hypertension, COPD/asthma, cardiovascular disease and disorders of the lipoprotein metabolism. This pattern was labeled *"Metabolic, pulmonary and cardiovascular disorders"*.

3.3. Function among patterns of multimorbidity at the three assessments

The densities of the DEMMI scores at the three time points and the baseline DEMMI score for the patients who died or dropped out are depicted in Fig. 2. For the patterns *"Minimal chronic conditions"*; *"Degenerative, lifestyle and mental disorders"; "Neurological, functional and sensory disorders"*; and *"Metabolic, pulmonary and cardiovascular disorders"*, respectively, 6, 1, 3, and 7 patients died between baseline and first assessment, and 20, 5, 19, and 13 patients died between first and second assessment, respectively. In addition, 14, 2, 10, and 2 patients dropped out between baseline and first assessment, and 15, 3, 10, and 4 patients dropped out between first and second assessment, respectively. We found that the patterns *"Neurological, functional and sensory disorders"* and *"Metabolic, pulmonary and cardiovascular disorders"* had a significant lower DEMMI score at baseline and the one-month assessment adjusted for age and sex than the *"Minimal chronic conditions"* pattern (Table 3). At the one-year assessment, only the "*Neurological, functional and sensory disorders*" pattern showed a significant lower DEMMI score adjusted for age and sex (Table 3). Furthermore, we found that the *"Neurological, functional and sensory disorders"* pattern showed a significant lower handgrip strength, gait speed and Barthel20 (adjusted for age and sex) at both baseline and at the one-year assessment and a lower NMS at the one-year assessment than the *"Minimal chronic conditions"* pattern (Table 3). We found no significant differences in function between the patterns *"Neurological, functional and sensory disorders"; "Degenerative, lifestyle and mental disorders";* and *"Metabolic, pulmonary and cardiovascular disorders" except for handgrip strength at baseline (p = 0.03* between *"Degenerative, lifestyle and mental disorders"* and *"Metabolic, pulmonary and cardiovascular disorders") and at the one-year assessment (p = 0.02* between *"Neurological, functional and sensory disorders"* and *"Metabolic, pulmonary and cardiovascular disorders")* and *for Barthel20 at the one-year assessment (p = 0.02* between *"Neurological, functional and sensory disorders"* and *"Metabolic, pulmonary and cardiovascular disorders"*).

3.4. Recovery profiles after an acute medical admission

In total, 144 patients in the *"Minimal chronic conditions"* pattern, 21 patients in the *"Degenerative, lifestyle and mental disorders"* pattern, 74 patients in the *"Neurological, functional and sensory disorders"* pattern, and 38 patients in the *"Metabolic, pulmonary and cardiovascular disorders"* pattern had a DEMMI score at baseline and at the one-month assessment. Furthermore, 105 patients in the *"Minimal chronic conditions"* pattern, 13 patients in the *"Degenerative, lifestyle and mental disorders"* pattern, 43 patients in the *"Neurological, functional and sensory disorders"* pattern, and 25 patients in the *"Metabolic, pulmonary and cardiovascular disorders"* pattern had a DEMMI score at the one-month assessment and at the one-year assessment. Compaired to the *"Minimal chronic conditions"* pattern we did not find a significant difference between patterns in change in DEMMI score from baseline to the one-month assessment nor from the one-month assessment to the one-year assessment (Table 3). From the baseline to the one-month assessment the *"Minimal chronic conditions"* pattern (p-value (adjusted for age, sex, and baseline DEMMI score): $p < 0.001$), the *"Neurological, functional and sensory disorders"* pattern (p = 0.1) and the *"Metabolic, pulmonary and cardiovascular disorders"* pattern (p = 0.3) improved in DEMMI score (Table 3). However, only the *"Minimal chronic conditions"* pattern had a significant improvement. The *"Degenerative, lifestyle and mental disorders"* pattern dropped in DEMMI score. However, this was not significant (p = 0.7) (Table 3).

4. Discussion

This study aimed to describe how function relates to different patterns of multimorbidity using latent class analysis in a population of acutely hospitalized medical patients aged 65 and above. We identified four patterns of multimorbidity based on the presence or absence of the 22 most prevalent chronic conditions representing different pathophysiology. These patterns differed significantly regarding mobility and functional outcomes assessed during the acute hospitalization, in the patients home one-month and one-year after discharge. Compaired to the *"Minimal chronic conditions"* pattern, we were not able to find any between-pattern differences in recovery profiles measured as the

Table 2
Conditional probabilities of the 22 chronic conditions within the four patterns in the LCA model, including pattern size and expected number of chronic conditions (n = 369).

Pattern label	Prevalence of chronic conditions	Minimal chronic conditions		Degenerative, lifestyle and mental disorders		Neurological, functional and sensory disorders		Metabolic, pulmonary and cardiovascular disorders	
Pattern size		0.54		0.05		0.25		0.16	
Expected number of chronic conditions		2.80		4.92		5.98		6.25	
Colitis ulcerosa/Chron´s disease	0.08	0.03		0.16		0.09		0.16	
Dementia	0.05	0.01		0.00		0.18		0.03	
Depression	0.06	0.02		0.17		0.13		0.03	
Diabetes	0.17	0.10/0.27[a]		0.15/0.38[a]		0.14/0.36[a]		0.42/0.71[a]	
Disability	0.06	0.01		0.15		0.18		0.00	
Brain infarction/hemorrhage	0.15	0.04		0.00		0.38		0.18	
Hypertension	0.41	0.11		0.34		0.81		0.74	
COPD/asthma	0.33	0.21		0.83		0.17		0.76	
Chronic kidney disease	0.05	0.00		0.12		0.10		0.13	
Neuropathy	0.05	0.01		0.30		0.10		0.00	
Osteoporosis/osteoarthrosis	0.43	0.34/0.17[b]		0.54/0.32[b]		0.58/0.36[b]		0.44/0.24[b]	
Parkinson disease	0.05	0.04		0.00		0.02		0.12	
Arthritis	0.14	0.07		0.31		0.22		0.14	
Disorders of the eyes and ears	0.32	0.20		0.33		0.59		0.31	
Mental disorders due to tobacco	0.05	0.01		0.34		0.00		0.12	
Thyroid dysfunction	0.12	0.09		0.17		0.21		0.06	
Mental disorders due to alcohol	0.04	0.01/0.02[b]		0.18/0.48[b]		0.06/0.21[b]		0.09/0.30[b]	
Obesity	0.05	0.02/0.17[a]		0.28/0.79[a]		0.03/0.21[a]		0.09/0.49[a]	
Gastritis	0.09	0.04		0.14		0.07		0.23	
Cardiac disease	0.48	0.27		0.30		0.71		0.83	
Disorders of the lipoprotein metabolism	0.60	0.51/0.68[b]		0.00/0.00[b]		0.67/0.81[b]		1.00/1.00[b]	
Genitourinary diseases	0.18	0.15/0.29[b]		0.05/0.11[b]		0.28/0.49[b]		0.20/0.37[b]	
Age, years; median (IQR)		77	(70;85)	75	(68;81)	79	(75;85)	76	(71;85)
Female; number (%)		119	(60)	14	(74)	63	(67)	34	(59)

Abbreviations: IQR = inter quartile range.
Note: [a] Conditional probabilities for patients aged 65/85 years. [b] Conditional probabilities for females/males. Parameter estimates for differential item function: Diabetes ON age = −0.061; Obesity ON age = −0.112; Disorders of the lipoprotein metabolism ON sex = −0.729; Mental disorders due to alcohol ON sex = −1.476; Osteoporosis/osteoarthrosis ON sex = 0.902; Genitourinary diseases ON sex = −0.876.

change in DEMMI after an acute hospitalization. Furthermore, we found significantly lower handgrip strength, gait speed, and Barthel20 for the *"Neurological, functional and sensory disorders"* pattern compared to the *"Minimal chronic conditions"* pattern at all three outcome assessments.

The four patterns of multimorbidity identified in this study should be interpreted with caution due to the explorative nature of the analysis. Notably, the aim of this study was not to identify patterns of multimorbidity but to use LCA as a multivariate model to investigate differences in function among acutely hospitalized patients. Nonetheless, the multimorbid patterns are comparable with previous systematic reviews which have found three groups of patterns across studies in both community-dwelling adults and elderly including 1) a combination of cardiovascular and metabolic diseases; 2) a combination of diseases concerning mental health; and 3) a combination of musculoskeletal disorders and/or pain (Prados-Torres et al., 2014; Violan et al., 2014). A recent systematic review investigating different analytical methods for measuring patterns of multimorbidity found similar patterns when applying five different methods, except for the combination of musculoskeletal disorders and/or pain which was replaced by a pattern of allergic diseases (Ng, Tawiah, Sawyer, & Scuffham, 2018). In our study, we were also able to find a pattern of cardiovascular and metabolic diseases (the *"metabolic, pulmonary and cardiovascular disorders"* pattern). However, we did not find two distinct patterns of diseases concerning mental health and of musculoskeletal disorders as these were combined in the *"Degenerative, lifestyle and mental disorders"* pattern and in the *"Neurological, functional and sensory disorders"* pattern. This might be caused by differences in sample size and/or included chronic conditions. Also, the population in this study were included in the Emergency Department whereas the populations in the systematic reviews were based on both the general population as well as patients. Therefore, this study has a higher degree of morbidity, which is reflected in the proportion of patients with multimorbidity (Table 1).

We found significant between-pattern differences for DEMMI at each of the three assessments of function. These results are in line with previous studies which also have found differences in function between patterns of multimorbidity (Guisado-Clavero et al., 2018b; Jackson et al., 2015; Koller et al., 2014; Marengoni, Angleman, & Fratiglioni, 2011; Marventano et al., 2014b; Olaya et al., 2017; Quiñones et al., 2016; Vetrano, Rizzuto et al., 2018). However, we did not find any studies in a population of acutely hospitalized older medical patients, and we found only one study using objective measures of function (Vetrano, Rizzuto et al., 2018). Vetrano et al. found that patterns of neuropsychiatric disorders had stronger associations with low level of activities of daily living and with slow gait speed than patterns of cardiovascular multimorbidity in a sample of 2,385 people aged 60 years or older participating in the Swedish National study of Ageing and Care in Kungsholmen (Vetrano, Rizzuto et al., 2018). In our study, we also found that the pattern described by high probabilities of neuropsychiatric conditions (*"Neurological, functional and sensory disorders"*), though more neurological than psychiatric conditions, had significantly lower mobility than the *"Minimal chronic diseases"* pattern. This difference was also clinically relevant at baseline and one-month follow-up visit, but not at the one-year assessment based on a 10-point difference in the DEMMI-score. Nonetheless, this pattern was the only pattern that differed significant from the *"Minimal chronic diseases"*

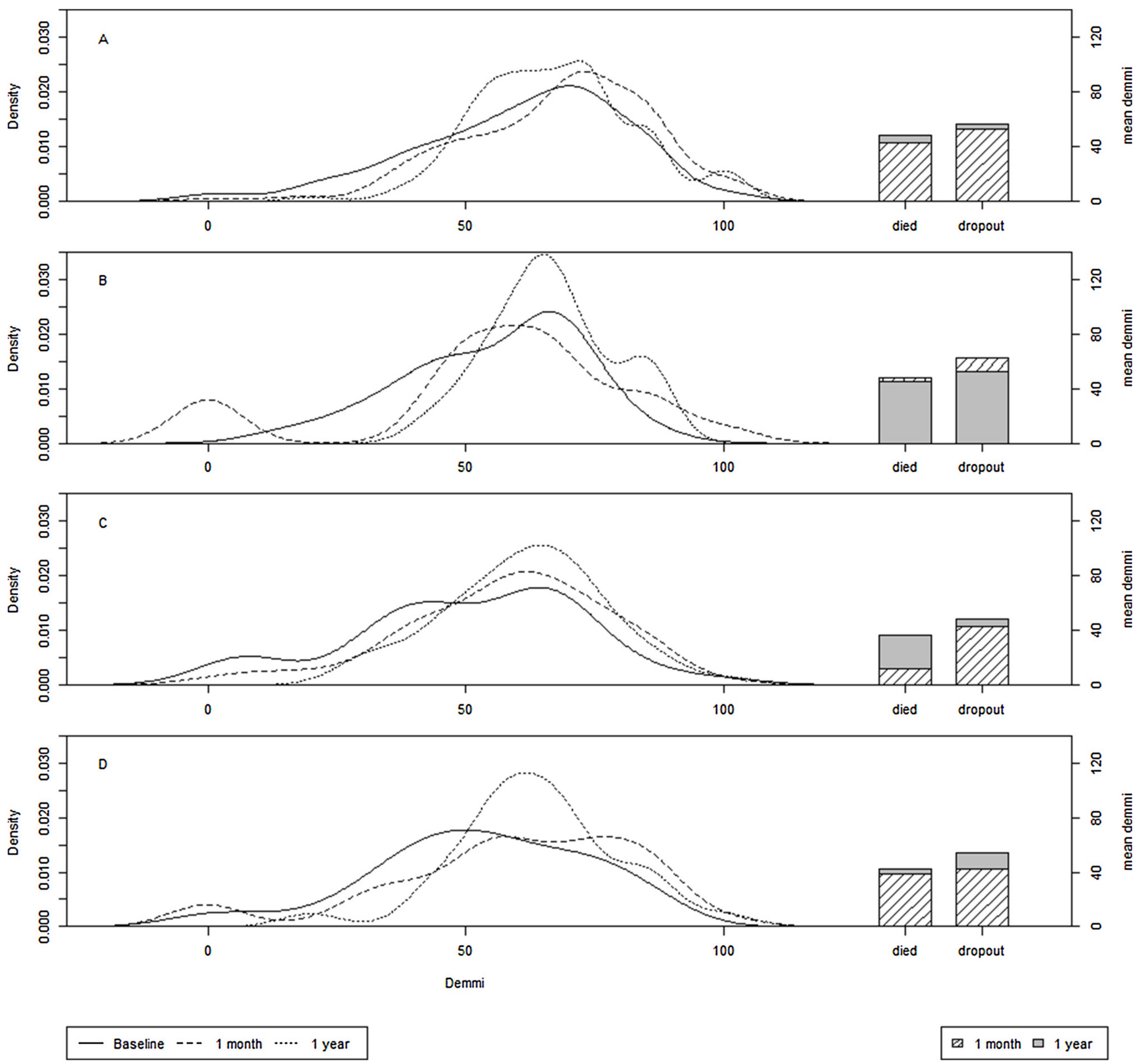

Fig. 2. Density plot of de Morton Mobility Index (DEMMI) score for the four patterns of mobility (A: Minimal chronic disease; B: Degenerative, lifestyle and mental disorders; C: Neurological, functional and sensory disorders; and D: Metabolic, pulmonary and cardiovascular disorders) and baseline DEMMI score for patients who died and who dropped out.

pattern regarding DEMMI at the one-year assessment. The *"Neurological, functional and sensory disorders"* pattern showed significant lower DEMMI-score, handgrip strength, gait speed, and Bathel20 than the *"Minimal chronic diseases"* pattern. This migth be caused by the pattern including a high conditional prevalence of disorders like brain infarction/hemorrhage and dementia affecting cognition, which have been asoociated with a a decline in mobility (Buchman, Boyle, Leurgans, Barnes, & Bennett, 2011). Studies should therefore investigate the effect of intensified rehabilitation to the *"Neurological, functional and sensory disorders"* pattern after an acute hospitalization. However, we were not able to distinguish the *"Neurological, functional and sensory disorders"* pattern from the patterns *"Degenerative, lifestyle and mental disorders" and "Metabolic, pulmonary and cardiovascular disorders"* regarding function, which is probably due to the low sample size. Further studies with a higher sample size are therefore warranted. Nevertheless, the results show that differences exist between the *"Minimal chronic diseases"* pattern and the other patterns, which suggests a differentiated approach to rehabilitation after an acute hospitalization.

All patterns except one improved from baseline to the one-month follow-up visit in the DEMMI score, however only the *"Minimal chronic conditions"* pattern showed significant improvements. A recent study from Norway also found an improvement in function measured by Timed Up and Go, handgrip strength and Barthel Index among older multimorbid patients after an acute hospitalization (three weeks) (Moen et al., 2018). This improvement in function is also seen during hospitalization in studies of +65-year-old acutely hospitalized patients (Bodilsen et al., 2013; De Buyser et al., 2014). In the present study, we found that the *"Minimal chronic conditions"* pattern, which also had the highest DEMMI score at baseline, improved most from baseline to the one-month follow-up. This might be an indicator of the higher level of the ability to recover from an acute illness, i.e. physical resilience in this group of patients (Whitson et al., 2016). But further studies with a more confirmative design are needed to study this.

We were not able to find any between-pattern differences in recovery profiles measured as change of DEMMI after an acute hospitalization. This might be caused by several factors. Firstly, it is possible

Table 3
Latent regression analysis for between-pattern differences in function adjusted for age and sex.

Variables	Patterns of multimorbidity										
	Minimal chronic conditions		Degenerative, lifestyle and mental disorders			Neurological, functional and sensory disorders			Metabolic, pulmonary and cardiovascular disorders		
					p-value[1]			p-value[1]			p-value[1]
DEMMI (points); mean(SE)											
Baseline	63.4	(2.0)	55.7	(3.5)	0.07	46.8	(3.0)	< 0.01	52.4	(3.7)	0.01
One month follow up	70.8	(1.7)	52.7	(6.1)	< 0.01	55.1	(2.6)	< 0.01	59.3	(4.2)	0.01
One-year follow up	69.0	(1.7)	66.2	(3.0)	0.74	59.0	(2.4)	< 0.01	62.9	(3.3)	0.11
Handgrip strength (kg); mean (SE)											
Baseline	27.6	(1.2)	17.7	(1.2)	< 0.01	17.4	(1.1)	< 0.01	23.0	(2.3)	0.09
One-year follow up	26.0	(1.2)	18.5	(1.8)	< 0.01	18.0	(1.0)	< 0.01	23.1	(1.9)	0.21
Gait speed (m/sec); mean (SE)											
Baseline	0.8	(0.0)	0.7	(0.1)	0.06	0.6	(0.0)	< 0.01	0.6	(0.0)	< 0.01
One-year follow up	0.8	(0.0)	0.7	(0.1)	0.60	0.6	(0.0)	< 0.01	0.7	(0.0)	0.05
Barthel20: mean (SE)											
Baseline	19.7	(0.1)	16.8	(0.9)	< 0.01	14.7	(0.7)	< 0.01	17.5	(1.2)	0.06
One-year follow up	19.4	(0.1)	16.8	(1.4)	0.05	15.7	(0.7)	< 0.01	18.0	(18.0)	0.01
NMS < 5; mean (SE)[2]											
Baseline	0.48	(0.04)	0.61	(0.10)	0.23	0.58	(0.05)	0.13	0.54	(0.08)	0.41
One-year follow up	0.49	(0.05)	0.50	(0.13)	0.95	0.32	(0.07)	0.05	0.29	(0.08)	0.04
Change in DEMMI[3]											
Baseline to one-month	6.1	(1.2)	−1.3	(3.8)	0.06	3.9	(2.5)	0.43	4.0	(4.5)	0.65
One-month to one-year	−2.9	(1.3)	1.9	(2.6)	0.11	−1.8	(1.3)	0.63	3.5	(4.1)	0.13

Note: [1] p-value for the difference between the given pattern and the "Minimal chronic conditions"-class adjusted for age and sex. (Zisberg et al., 2015) Mean corresponds to the percentage of patients with a NMS < 5 [3] Only patients with a DEMMI score at both time point are included in the analysis. Abbreviations: IQR = interquartile range; DEMMI = de Morton Mobility Index; SE = Standard error; NMS = New Mobility Score.

that the explorative nature of the study has selection bias, since the *"Degenerative, lifestyle and mental disorders"* pattern only included data from ten patients on the DEMMI score at the one-year assessment due to dropouts and mortality, and the patients dying or dropping out had a lower DEMMI-score at baseline. Secondly, as this is a secondary analysis powered to detect differences in mobility between two proportions (Bodilsen et al., 2016), it is possible that the number of patients included in the analyses is too small to detect a difference in DEMMI change scores between patterns.

Gait speed has previously been found feasible and reliable in acutely hospitalized older medical patients (Bodilsen et al., 2015) and has been found to be able to discriminate between different patterns of multimorbidity (Vetrano, Rizzuto et al., 2018). In this study, we found that the *"Neurological, functional and sensory disorders"* pattern showed a significant lower gait speed than the *"Minimal chronic conditions"* pattern at both baseline and the one-year assessment and that the *"Metabolic, pulmonary and cardiovascular disorders"* pattern showed a significant lower gait speed at baseline. Slow gait speed is a strong predictor of early death, disability, falls and hospitalization/institutionalization in older people living in a community setting (Pamoukdjian et al., 2015) and is recommended to be used in a hospital setting in the first guideline for the clinical assessment and management of multimorbidity issued by (National Institute for Health and Care Excellence (NICE) (2016)).

4.1. Strengths and limitations

The strengths of this study are the objective measure of mobility, completeness of data due to the use of registry data for determining multimorbidity, which eliminates recall bias. Several limitations should also be noted. Firstly, it is possible that an underreporting of some chronic conditions has occurred. Multimorbidity diagnoses were mainly based on routine clinical discharge registrations as well as registrations from outpatient visits with the possibility of miscoding as not all secondary ICD10-codes are registered. Nonetheless, we have included data from national registers with a 10-year history as suggested by Juul-Larsen et al. (2019) and Schram et al. (2008) as well as used data from prescription medicine to define chronic conditions, which decreases the risk of misclassification. Additionally, the grouping of the 83 chronic conditions from the Chronic Condition Measurement Guide into 35 conditions based on the pathophysiology further decreases the risk of misclassification. Secondly, due to the number of dropouts and the difference in mobility measures for the group of patients who died during the follow-up, it is possible that attrition bias has been introduced. Hence, the external validity of the results can be affected, and results are therefore restricted to this selected patient group. In addition, a high percentage of the patients declined to participate, and the many eligibility criteria further decreases the generalizability. Thirdly, due to the exploratory nature of this study the patterns of multimorbidity should be interpreted with caution. We have used LCA as a multivariate model to investigate the differences in function between patterns of multimorbidity, however, more confirmative studies with a higher sample size should be conducted in order to identify validated patterns of multimorbidity. In addition, the labeling of the patterns were based on which conditions exhibited excess prevalence. Other ways of labeling could have been used, ex. based on the most prevalent combinations of chronic conditions within each pattern, which could have resulted in other labels. Therefore, the labels of the four patterns should be interpreted with caution.

5. Conclusion

In conclusion, these findings support that acutely hospitalized older medical patients with different patterns of multimorbidity differ with regards to function at three different time points; at acute medical hospitalization, one month and one year after discharge. The *"Neurological, functional and sensory disorders"* pattern showed a significantly lower level of function in all outcomes than the *"Minimally chronic conditions"* patterns, which suggests that a differentiated approach based on patterns of multimorbidity regarding rehabilitation strategies after an acute hospitalization must be a priority in future studies, but also that studies should investigate the effect of intensified rehabilitation to the *"Neurological, functional and sensory disorders"* pattern after an acute hospitalization. In addition, compaired to the *"Minimal chronic conditions"* pattern, we did not find any between-pattern differences in recovery profile, measured as change in mobility after discharge. We did, however, find significantly within-pattern change in mobility and hence, recovery profiles after acute hospitalization for the *"Minimally chronic conditions"* pattern, but this was on average not clinically relevant. Further investigation of the effect of different multimorbidity patterns on recovery profiles after an acute hospitalization is needed to accommodate a tailored approach towards treatment and rehabilitation among acutely hospitalized older medical patients with multimorbidity.

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CRediT authorship contribution statement

Helle Gybel Juul-Larsen: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Data curation, Writing - original draft, Writing - review & editing, Visualization, Supervision, Project administration. **Ove Andersen:** Conceptualization, Methodology, Investigation, Resources, Writing - review & editing, Supervision. **Thomas Bandholm:** Conceptualization, Methodology, Writing - review & editing, Supervision. **Ann Christine Bodilsen:** Methodology, Investigation, Writing - review & editing. **Thomas Kallemose:** Methodology, Software, Validation, Formal analysis, Data curation, Writing - review & editing, Visualization. **Lillian Mørch Jørgensen:** Methodology, Writing - review & editing. **Henrik Hedegaard Klausen:** Methodology, Investigation, Writing - review & editing. **Hanne Gilkes:** Investigation, Writing - review & editing. **Janne Petersen:** Conceptualization, Methodology, Software, Validation, Formal analysis, Data curation, Writing - review & editing, Visualization, Supervision, Project administration.

Declaration of Competing Interest

None.

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Appendix A. Supplementary data

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